

CLAIMS

1. A tumor necrosis factor mutant protein, where one or more amino acid residues selected from the group consisting of the 29th, 31st, 32nd, 145th, 146th and 147th amino acid residues, or the group consisting of the 84th to 89th amino acid residues from the N-terminal of the amino acid sequence of SEQ ID NO:1 are replaced with other amino acid(s).
10 2. The tumor necrosis factor mutant protein of claim 1, which has an antagonistic activity against tumor necrosis factor,

where the 29th amino acid residue from the N-terminal of the amino acid sequence of SEQ ID NO:1 is replaced with arginine, histidine or serine; the 31st amino acid residue replaced with arginine, asparagine, glutamic acid, proline or serine; the 32nd amino acid residue replaced with histidine, methionine, threonine or tyrosine; the 145th amino acid residue replaced with alanine, asparagine, aspartic acid or serine; the 146th amino acid residue replaced with asparagine, glycine, methionine or serine; and the 147th amino acid residue replaced with alanine, asparagine, proline, threonine or a stop codon;

where the 145th amino acid residue is replaced with alanine, lysine or arginine; the 146th amino acid residue replaced with glutamic acid, asparagine, aspartic acid or threonine; and the 147th amino acid residue replaced with threonine or aspartic acid; or

where the 84th amino acid residue is replaced with alanine, threonine, serine or glycine; the 85th amino acid

residue replaced with proline, threonine or glycine; the 86th amino acid residue replaced with alanine, glycine, threonine or proline; the 87th amino acid residue replaced with tyrosine, isoleucine or histidine; the 88th amino acid 5 residue replaced with glutamine, asparagine or serine; and the 89th amino acid residue replaced with arginine, histidine or glutamine.

3. The tumor necrosis factor mutant protein of claim 1, which has an agonist activity against tumor necrosis factor, 10 where the 29th amino acid residue from the N-terminal of the amino acid sequence of SEQ ID NO:1 is replaced with leucine, glutamine, threonine or lysine; the 31st amino acid residue replaced with arginine, glycine, serine or alanine; the 32nd amino acid residue replaced with tryptophan, tyrosine, aspartic acid or glycine; the 146th amino acid residue replaced with glutamic acid, alanine or serine; and the 147th amino acid residue replaced with serine, arginine or threonine; or

where the 84th amino acid residue is replaced with 20 threonine, serine or asparagine; the 85th amino acid residue replaced with serine, lysine, proline, tyrosine, arginine, threonine, histidine, glutamic acid, aspartic acid or alanine; the 86th amino acid residue replaced with histidine, threonine, leucine, asparagine, alanine, valine, 25 lysine, serine, glutamine, glycine, arginine or aspartic acid; the 88th amino acid residue replaced with serine, proline, threonine, asparagine, alanine, glycine, arginine or glutamine; and the 89th amino acid residue replaced with aspartic acid, histidine, lysine, glycine, serine, proline, 30 alanine, glutamine, phenylalanine or arginine.

4. The tumor necrosis factor mutant protein of claim 2, which is a protein comprising an amino acid sequence selected from the group consisting of SEQ ID NOs:9 to 22 or optionally where one or more amino acid residues selected
5 from the group consisting of the 11th, 65th, 90th, 98th, 112th and 128th amino acid residues from the N-terminal of said amino acid sequence are replaced with lysine residues, and having an antagonistic activity against tumor necrosis factor.
- 10 5. The tumor necrosis factor mutant protein of claim 3, which is a protein comprising an amino acid sequence selected from SEQ ID NOs:37 to 59 or optionally where one or more amino acid residues selected from the group consisting of the 11th, 65th, 90th, 98th, 112th and 128th
15 amino acid residues from the N-terminal of said amino acid sequence are replaced with lysine residues, and having an agonistic activity against tumor necrosis factor.
6. The tumor necrosis factor mutant protein of claim 1, which conjugates with a water-soluble polymer.
- 20 7. The tumor necrosis factor mutant protein of claim 6, wherein said water-soluble polymer is polyethylene glycol.
8. A tumor necrosis factor inhibitor, which comprises the tumor necrosis factor mutant protein of claim 2.
9. A tumor necrosis factor preparation, which comprises
25 the tumor necrosis factor mutant protein of claim 3.